

WHAT IS CLAIMED IS:

1. A method for sterilizing a preparation containing albumin that is sensitive to radiation, said method comprising:

(i) adding to said preparation containing albumin at least one stabilizer in an amount effective to protect said preparation containing albumin from said radiation; and

(ii) irradiating said preparation containing albumin with a suitable radiation at an effective rate for a time effective to sterilize said preparation containing albumin.

2. A method for sterilizing a preparation containing albumin that is sensitive to radiation, said method comprising:

(i) reducing the residual solvent content of said preparation containing albumin to a level effective to protect said preparation containing albumin from said radiation; and

(ii) irradiating said preparation containing albumin with a suitable radiation at an effective rate for a time effective to sterilize said preparation containing albumin.

3. A method for sterilizing a preparation containing albumin that is sensitive to radiation, said method comprising:

(i) reducing the temperature of said preparation containing albumin to a level effective to protect said preparation containing albumin from said radiation; and

(ii) irradiating said preparation containing albumin with a suitable radiation at an effective rate for a time effective to sterilize said preparation containing albumin.

4. A method for sterilizing a preparation containing albumin that is sensitive to radiation, said method comprising:

(i) applying to said preparation containing albumin at least one stabilizing process selected from the group consisting of

- (a) reducing the residual solvent content of said preparation containing albumin,
- (b) reducing the temperature of said preparation containing albumin, and
- (c) adding at least one stabilizer to said preparation containing albumin; and

5 (ii) irradiating said preparation containing albumin with a suitable radiation at an effective rate for a time effective to sterilize said preparation containing albumin, wherein said at least one stabilizing process and the rate of irradiation are together effective to protect said preparation containing albumin from said radiation.

10 5. A method for sterilizing a preparation containing albumin that is sensitive to radiation, said method comprising:

(i) applying to said preparation containing albumin at least two stabilizing processes selected from the group consisting of

- (a) reducing the residual solvent content of said preparation containing albumin,
- (b) reducing the temperature of said preparation containing albumin, and
- (c) adding at least one stabilizer to said preparation containing albumin; and

15 (ii) irradiating said preparation containing albumin with a suitable radiation at an effective rate for a time effective to sterilize said preparation containing albumin, wherein said at least two stabilizing processes are together effective to protect said preparation containing  
20 albumin from said radiation and further wherein said at least two stabilizing processes may be performed in any order.

6. The method according to claim 2, 4 or 5, wherein said solvent is water.

7. The method according to claim 6, wherein said residual water content is reduced by the addition of an organic solvent.

8. The method according to claim 2, 4 or 5, wherein said solvent is an organic solvent.
9. The method according to claim 2, 4 or 5, wherein said preparation containing albumin is suspended in an organic solvent following reduction of said residual solvent content.
10. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is not more than about 3.0 kGy/hour.
11. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is not more than about 2.0 kGy/hr.
12. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is not more than about 1.0 kGy/hr.
13. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is not more than about 0.3 kGy/hr.
14. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is more than about 3.0 kGy/hour.
15. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is at least about 6.0 kGy/hour.
16. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is at least about 18.0 kGy/hour.
17. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is at least about 30.0 kGy/hour.
18. The method according to claim 1, 2, 3, 4 or 5, wherein said effective rate is at least about 45 kGy/hour.
19. The method according to claim 1, 2, 3, 4 or 5, wherein said preparation containing albumin is maintained in a low oxygen atmosphere.

20. The method according to claim 1, 2, 3, 4 or 5, wherein said preparation containing albumin is maintained in an atmosphere comprising at least one noble gas.

21. The method according to claim 20, wherein said noble gas is argon.

22. The method according to claim 1, 2, 3, 4 or 5, wherein said preparation containing  
5 albumin is maintained in a vacuum.

23. The method according to claim 2, 4 or 5, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of solute, evaporation, chemical extraction, spray-drying, and vitrification.

24. The method according to claim 2, 4 or 5, wherein said residual solvent content is less  
10 than about 15%.

25. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 10%.

26. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 3%.

15 27. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 2%.

28. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 1%.

20 29. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 0.5%.

30. The method according to claim 2, 4 or 5, wherein said residual solvent content is less than about 0.08%.

31. The method according to claim 1, 2, 3, 4 or 5, wherein at least one sensitizer is added to said preparation containing albumin prior to said step of irradiating said preparation containing albumin.

5 32. The method according to claim 1, 2, 3, 4 or 5, wherein said preparation containing albumin contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, prions or similar agents responsible, alone or in combination, for TSEs and single or multicellular parasites

33. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is an antioxidant.

10 34. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is a free radical scavenger.

35. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is a combination stabilizer.

36. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is a ligand.

15 37. The method according to claim 36, wherein said ligand is heparin.

38. The method according to claim 1, 4 or 5, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

39. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; 6-hydroxy-  
20 2,5,7,8-tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate and mixtures of two or more thereof.

40. The method according to claim 39, wherein said mixtures of two or more additional stabilizers are selected from the group consisting of: mixtures of ascorbic acid, or a salt or ester  
25 thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester

thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; and mixtures of uric acid, or a salt or ester thereof; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

41. The method according to claim 1, 4 or 5, wherein said at least one stabilizer is a dipeptide stabilizer.

42. The method according to claim 41, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine and anserine.

43. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is corpuscular radiation or electromagnetic radiation, or a mixture thereof.

44. The method according to claim 43, wherein said electromagnetic radiation is selected from the group consisting of radio waves, microwaves, visible and invisible light, ultraviolet light, x-ray radiation, gamma radiation and combinations thereof.

45. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is gamma radiation.

46. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is E-beam radiation.

47. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is visible light.

48. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is ultraviolet light.

49. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is x-ray radiation.

50. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is polychromatic visible light.

51. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is infrared.

52. The method according to claim 1, 2, 3, 4 or 5, wherein said radiation is a combination of one or more wavelengths of visible and ultraviolet light.

53. The method according to claim 1, 2, 3, 4 or 5, wherein said irradiation is conducted at ambient temperature.

5 54. The method according to claim 1, 2, 3, 4 or 5, wherein said irradiation is conducted at a temperature below ambient temperature.

55. The method according to claim 1, 2, 3, 4 or 5, wherein said irradiation is conducted below the freezing point of said preparation containing albumin.

56. The method according to claim 1, 2, 3, 4 or 5, wherein said irradiation is conducted below the eutectic point of said preparation containing albumin.

57. The method according to claim 1, 2, 3, 4 or 5, wherein said irradiation is conducted at a temperature above ambient temperature.

58. A composition comprising at least one preparation containing albumin and at least one stabilizer in an amount effective to preserve said preparation containing albumin for its intended use following sterilization with radiation.

59. A composition comprising at least one preparation containing albumin, wherein the residual solvent content of said preparation containing albumin is at a level effective to preserve said preparation containing albumin for its intended use following sterilization with radiation.

60. The composition of claim 59, wherein said residual solvent content is less than about 15%.

61. The composition of claim 59, wherein said residual solvent content is less than about 10%.

62. The composition of claim 59, wherein said residual solvent content is less than about 5%.

63. The composition of claim 59, wherein said residual solvent content is less than about 2%.

64. The composition of claim 59, wherein said residual solvent content is less than about 1%.

65. The composition of claim 59, wherein said residual solvent content is less than about 0.5%.

66. The composition of claim 59, wherein said residual solvent content is less than about 0.08%.

67. The composition of claim 58 or 59, wherein said preparation containing albumin is glassy or vitrified.

68. The composition of claim 58 or 59, wherein said preparation containing albumin further comprises at least one protein selected from the group consisting of monoclonal immunoglobulins, polyclonal immunoglobulins, glycosidases, sulfatases, urokinase, thrombin and Factor VIII.

69. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 0.5%.

70. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 1%.

71. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 5%.

72. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 10%.

73. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 15%.

74. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 20%.



75. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 25%.

76. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is at least about 50%.

5 77. The composition of claim 59, wherein the protein concentration of said preparation containing albumin is effective to protect said preparation containing albumin from radiation.

78. The method according to claim 6, wherein said preparation containing albumin is suspended in an organic solvent following reduction of said residual solvent content.

79. A method of treating hypovolemic shock comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

80. A method of treating burns comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

81. A method of maintaining fluid volume in a human undergoing cardiopulmonary bypass comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

82. A method of treating acute liver failure comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

83. A method of preventing the sequestration of protein rich fluids in a patient suffering from a condition selected from the group consisting of acute peritonitis, pancreatitis, mediastinitis and excessive cellulitis, said method comprising administering to a human in need thereof an

effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

84. A method of treating hypoalbumenemia comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

85. A method of treating hypoproteinemia with or without edema comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

86. A method of treating adult respiratory distress syndrome comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

87. A method of treating neonatal hemolytic disease comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

88. A method of treating acute nephrosis comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

89. A method of preventing shock or hypotension in a human undergoing renal dialysis comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

90. A method of treating shock due to burns, crushing injuries, abdominal emergencies, dehydration, infection or other cause where there is predominantly a loss of plasma fluid and not

red blood cells, said method comprising administering to a human in need thereof an effective of claim 1, 2, 3, 4 or 5.

91. A method of treating shock due to haemorrhage comprising administering to a human in need thereof an effective amount of a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

92. An improvement in a method of culturing cells, wherein said improvement comprises adding to the growth medium for said cells a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

93. An improvement in a method of producing a product of cell metabolism by culturing cells, wherein said improvement comprises adding to the growth medium for said cells a preparation containing albumin which has been sterilized according to the method of claim 1, 2, 3, 4 or 5.

94. The method according to claim 93, wherein said product is a protein.

95. The method according to claim 93, wherein said product is a recombinant protein.

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96. The composition of claim 58 or 59, wherein said preparation containing albumin further comprises at least one biological material selected from the group consisting of hemoglobin, anti-thrombin III, polysaccharides, vaccines, collagen, gelatin, trypsin, fetal bovine serum, transferring, insulin, human growth hormone, Factor IX, fibrinogen, Factor XIII, Factor XIIIa, Factor VII, Factor VIIa, growth factors, immunotoxins, bone morphogenetic proteins, osteogenic proteins, cytokines, Factor XI and plasma.

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